
A Green Catalytic System for the Knoevenagel Condensation using WEPBA

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ABSTRACT

An economical and eco-friendly method has been developed for Knoevenagel condensation of various aromatic aldehydes with active methylene compound malononitrile in water extract of papaya bark ash (WEPBA) as a basic green catalyst is described. The condensation found faster, efficient method, during stirring observed precipitation of the product. The isolated product is recrystallized and characterized by FT-IR, ¹H-, ¹³C-NMR spectroscopy.

Keywords

Knoevenagel condensation, WEPBA, green catalysis, water extract, aldehydes, malononitrile.

INTRODUCTION

In 1890 Emil Knoevenagel demonstrated the synthesis of substituted alkenes by the condensation of aldehydes with active methylene compounds in the presence of base. The condensation of aldehydes with active methylene compounds like malononitrile, ethylcyano acetate etc. shows very important and widely employed method in the series of carbon-carbon bond formation in organic synthesis^[1]. It has also been used in the preparation various intermediate of pharmacological application such as antiphosphorylation inhibition of EGF-receptor and anti-proliferative activity. Because of their bioactive importance and synthetic point of view a large number of methods for the Knoevenagel condensation have also been reported using various Lewis acids/bases, ultrasound, microwave, solid phase, ionic liquid or using green solvent like water and grindstone method under solvent free condition. The literature revealed use of various catalysts like amines and its corresponding ammonium salts, TiCl₄/base, ZnCl₂, BiCl₃, CdI₂, Al₂O₃, Ni-SiO₂, MgO, ZnO, AlPO₄-Al₂O₃, KF-Al₂O₃, natural phosphate and synthetic phosphate are employed⁽²⁻⁵⁾. However, the use of such bases/acids and solvents in large scale reactions has led to environmental issues, thus there is necessarily dispose of huge amounts of organic waste due to the formation of undesirable side products resulting from polymerization, *bis*-addition and self-condensation reactions. As a result other modified inorganic solids, resins, phase-transfer agents, ionic liquid, LDH-F hydrotalcite, cation-exchanged zeolites, or mesoporous materials, and MCM-41 have also been introduced as new catalysts⁽⁷⁻¹⁰⁾. Nevertheless, most of these known methods suffer from significant limitations, which include toxic reagents, harsh reaction conditions, low yields and longer reaction times.

In recent years, the classical organic chemistry had been revised to go for green approaches in the chemical industry, which are environmentally acceptable. Utpal Bora *et al.*, group reported the extraction of WEPBA and also showed elements present in it using EDX. The EDX spectra revealed

high distribution of the oxides of Na, Mg, K and Ca. Since, metal oxides can react with water to produce metal hydroxides, the above result highlights the basicity of the water extract⁽⁶⁾. To confirm this, we investigated first time for the Knoevenagel condensation reaction, which is depended on the presence of external base. The present work concern about environmental demand and development of an eco-friendly, non-hazardous method for the formation of carbon-carbon bond using inexpensive natural feedstock extract of papaya bark ash as a natural catalyst with excellent yield.

RESULT AND DISCUSSION

The condensation of organic aldehyde derivative with active methylene compound malononitrile is the classical example of a Knoevenagel reaction. The reaction requires basic media due to abstraction of a proton from the active methylene of malononitrile group. Researchers in the literature employed several inorganic bases such as NaOH, KOH, Na₂CO₃, K₂CO₃, NaHCO₃ in presence of other additives for the reaction^[11-16]. Weak bases are also used to perform reaction under homogeneous conditions and also in heterogeneous catalysts such as basic aluminium oxide, functionalized silica gel with alkyl amine and more are reported for the synthesis. In this work, we are exploring the utility of natural feedstock of papaya bark as a natural source for the condensation reaction. Recently Utpal bora and *etal* have reported a greener method for the Suzuki–Miyaura coupling reaction using WEPBA^[6] as a green basic media. The added advantage of WEPBA is used directly as a media without addition of organic solvent as well base. It is a green protocol for the synthesis and found reaction is faster with the isolation of product in excellent yield (**Table 1, Scheme 1**). In Table 1 showed, the aromatic aldehydes with different substituents such as Methoxy, Fluoro, Chloro, Bromo and *N,N*-Dimethyl benzaldehyde are used for the demonstration of this reaction. It is observed that, when electron withdrawing group present on benzaldehyde reaction found to be faster by 10-15min compared to electron donating group on it take more time for the completion of the reaction⁽¹⁹⁾. Extension of this reaction to ketone family fails because of their sterically hindered structure. In summary, we have developed a natural source as an inexpensive, simple and efficient method for the Knoevenagel condensation of aldehyde derivatives with malononitrile at room temperature stirring. The extension of Knoevenagel condensation product with synthetic application towards biologically active molecule synthesis is now in progress.

MATERIAL AND METHOD

Melting points were determined in open capillaries and are uncorrected. Reagents grade chemicals were purchased from commercial sources and used as received without further purification. IR spectra were recorded in KBr disks on a Shimadzu FT-IR, ¹H- and ¹³C-NMR spectra were recorded on a Bruker 300 (300 MHz) spectrometer using TMS as internal standard. The progress of the reaction was monitored by TLC. Yields refer to isolated pure products.

PREPARATION OF WEPBA

We adopted reported protocol⁽⁶⁾, briefly preparation of water extract of papaya bark ash (WEPBA) by burning agro waste papaya bark to ashes. After that, 10 g of ash was suspended in 100 ml of distilled water and stirred for one hour at room temperature. The suspension was then filtered and a lightyellow colored separated filtrate is termed as WEPBA.

Figure 1. FT-IR spectrum of Benzylidinemalononitrile

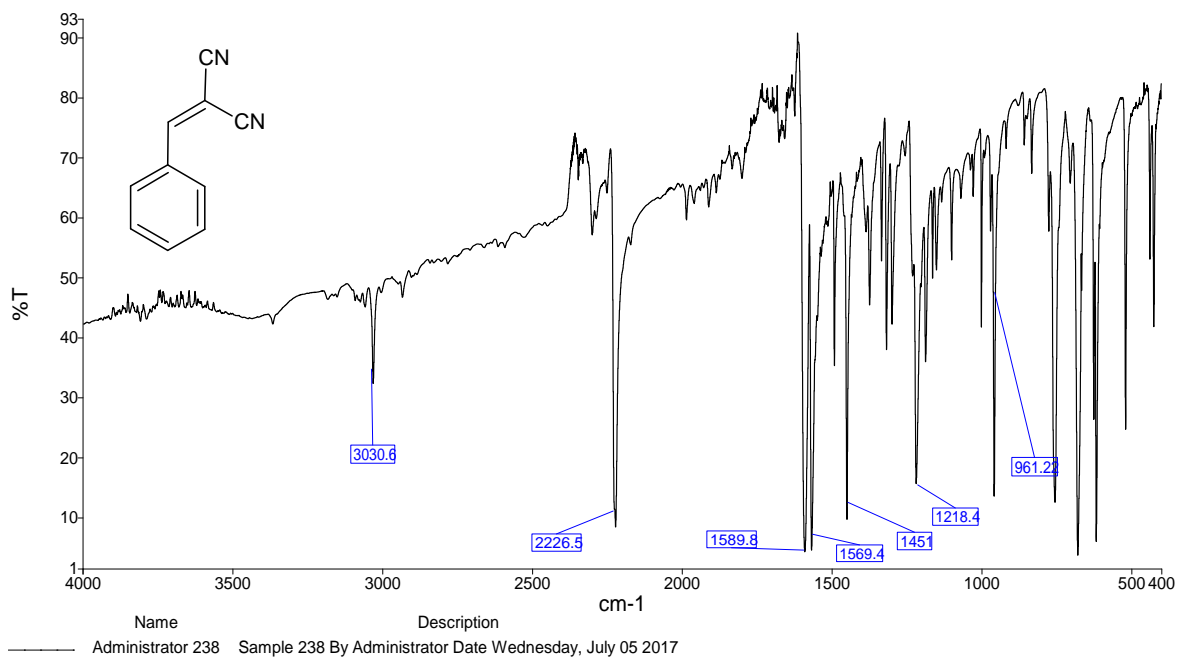
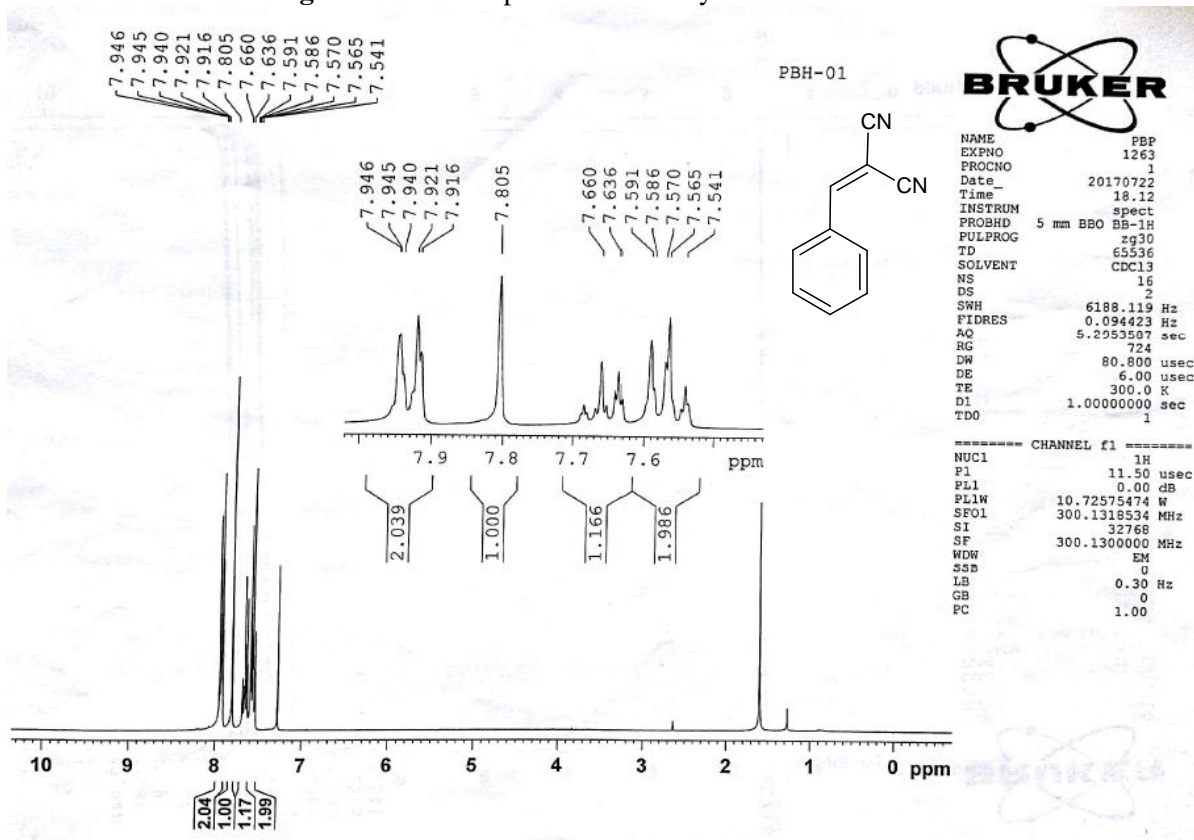


Figure 2. ¹H-NMR spectrum of Benzylidinemalononitrile



Scheme -1: General reaction of Knoevenagel reaction

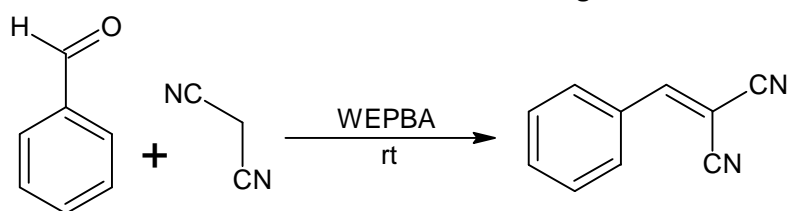
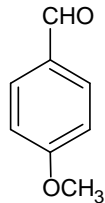
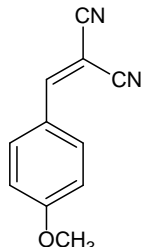
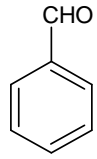
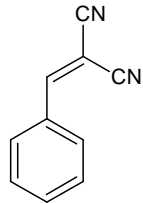
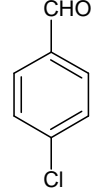
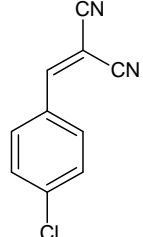
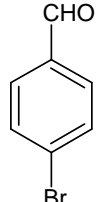
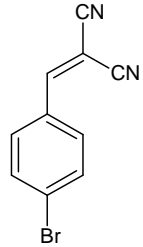
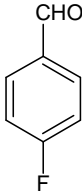
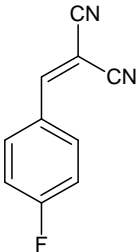
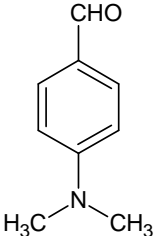
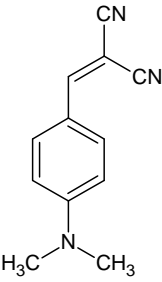
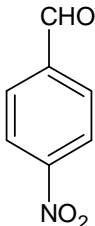
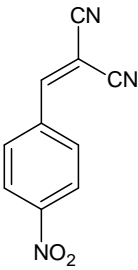
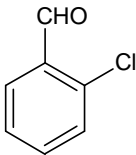
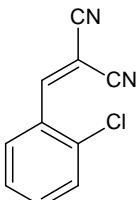
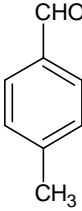
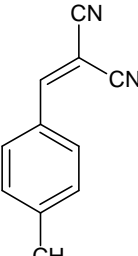
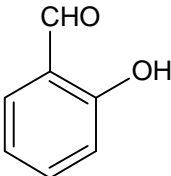
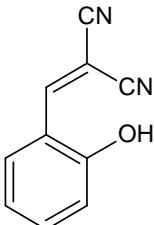


Table 1. Physical constant and reaction data of Knoevenagel product.

Entry	Aldehyde	Product*	Time (min)	mp (°C)	Yield (%) **
1			50	115-116	85
2			55	81-83	84
3			40	163-164	87
4			40	156-157	90

5			35	125-127	89
6			55	182-183	90
7			50	157-158	88
8			45	78-80	87
9			50	164-66	86
10			55	157-159	84

*All the products were characterized by ^1H -, ^{13}C NMR and FT-IR and comparison of m.p with literature data.

**Yields refer to the isolated yields.

CONCLUSION:

Herein we have developed an inexpensive, faster and greener method for Knoevenagel condensation of aromatic aldehydes with malononitrile using WEPBA as a green basic catalyst at room temperature. This procedure offers several advantages including shorter reaction time, clean reactions, easy work-up, and it is free from usage of organic solvents.

SOME SELECTED SPECTRAL DATA

2-[(4-Methoxyphenyl) methylene] malononitrile (entry 1): Pale yellow crystals, yield: 85%, mp 115-116°C (Lit: 114-115°C), FT-IR (KBr) 2218 (CN), 1598 (C=C). ^1H -NMR (300 MHz, CDCl_3 , 25°C): d = 7.92 (d, $J=8.5$ Hz, 2H, phenyl), 7.63 (s, 1H, CH), 7.2 (d, $J=8.5$ Hz, 2H, phenyl), 3.9 (s, 3H, OCH_3) ppm.

2-(Phenylmethylene) malononitrile (entry 2): Light yellow crystal, yield: 84%, mp 81-83°C (Lit: 82-83°C). FTIR (KBr) 3030 cm^{-1} (HC=C), 2226 cm^{-1} (CN), 1589 cm^{-1} (C=C). ^1H -NMR (300 MHz, CDCl_3): 7.91-7.94 (d, $J=8.5$ Hz, 2 H, phenyl), 7.8 (s, 1 H, CH), 7.54-7.66 (m, 3 H, phenyl) ppm.

2-[(4-Chlorophenyl) methylene] malononitrile (entry 3): Colorless crystals, yield: 87%, mp 165°C (Lit: 163-165°C). FTIR (KBr) 2223 (CN), 1582 (C=C). ^1H -NMR (300 MHz, CDCl_3): d = 7.84 (d, $J=8.4$ Hz, 2H, phenyl), 7.73 (s, 1H, CH), 7.5 (d, $J=8.4$ Hz, 2H, phenyl) ppm.

2-(4-Fluorophenylmethylene)malononitrile (entry 5): White solid; mp: 123-125°C (Lit: 121- 23°C), yield: 89% ^1H NMR (400 MHz, CDCl_3): = 7.97 (dd, $J=8.7, 5.2$ Hz, 2H), 7.77 (s, 1H), 7.25 (dd, $J=14.2, 5.78$ Hz, 2H); ^{13}C NMR (100 MHz, CDCl_3): = 165.82, 159.42, 133.48, 133.39, 127.38, 117.33, 117.17, 113.64, 112.5, 82.38.

2-(4-nitrobenzylidene)malononitrile (entry 7): mp: 158-159°C (Lit: 157-59°C); yield: 88% ^1H -NMR (400 MHz, CDCl_3): (ppm): 8.41 (d, $J=8.84$, 2H), 8.10 (d, $J=8.84$, 2H), 7.90 (s, 1H); ^{13}C -NMR (100 MHz, CDCl_3) (ppm): 156.8, 150.4, 135.8, 131.3, 124.6, 112.6, 111.5, 87.5.

2-(2-chlorobenzylidene)malononitrile (entry 8): mp: 79-82°C (Lit: 80-82°C); yield: 87% ^1H -NMR (400 MHz, CDCl_3): (ppm): 7.80 (d, $J=7.84$, 2H), 7.74 (s, 1H), 7.71 (d, $J=7.84$, 2H); ^{13}C -NMR (100 MHz, CDCl_3) (ppm): 158.4, 133.1, 131.8, 129.9, 129.6, 113.4, 112.3, 83.5.

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GENERAL PROCEDURE

A mixture of aromatic aldehydes (1 mmol), malononitrile (1 mmol), and WEPBA (5mL) taken in 10mL round bottomed flask and stirred at room temperature till completion of the reaction monitored by TLC. The product was filtered, recrystallized from ethanol, and dried at ambient temperature. The pure compound is subjected to spectroscopic method (FT-IR, NMR) and also determined physical constant, the melting point observed by this method is comparable with the literature data